

## **REMARKS**

Claims 46, 47, 49, 50, 77-89, 92, 93, 95-100, 107-108, 114, 120 and 151-157 are pending in the present application. Applicants respectfully request reconsideration in view of the following remarks.

Applicants thank the examiner for the indication that claim 151 is presently allowable and that claim 83 would be allowable if rewritten as an independent claim.

### **I. THE PENDING CLAIMS COMPLY WITH 35 USC §112, 1<sup>ST</sup> PARAGRAPH**

Applicants note with appreciation that the Examiner considers the claimed subject matter to be fully enabled and in compliance with 35 U.S.C. §112, first paragraph. Accordingly, none of the above amendments are made to overcome an issue concerning enablement, written description or best mode.

### **II. THE CLAIMED SUBJECT MATTER IS NOT ANTICIPATED BY THE ART**

#### **U.S. Patent No. 6,514,497 to Briskin et al. (the '497 patent)**

The Examiner has rejected claims 46, 49, 77-82, 84, 85, 114, 120 and 153 as anticipated by the '497 patent under 35 U.S.C. § 102(e). The '497 patent was filed on Oct. 1, 1998 after the filing date of the present application, however the '497 does claim the benefit of a provisional application 60/060,757 filed October 2, 1997.

The Examiner argues that the '497 patent teaches, "interaction of LERK-2 [ephrin B1] with its receptors results in angiogenesis" and "assays for inhibitors and promoters of LERK-2 mediated cell adhesion". The Examiner further argues, "That Applicant's method includes the mental step of selecting the receptor and ligand based on cell expression does not change the method itself. The resulting method uses the same receptors for the same purpose."

Applicants respectfully disagree with this rejection on the grounds that the '497 patent does not disclose all the elements of the claims, particularly the claims as amended. Applicants reserve the right to file a Declaration pursuant to 37 CFR 1.131 to demonstrate invention prior to

the filing date of the 60/060,757 provisional application, although given that the '497 patent does not anticipate the claims, such Declaration is not needed at this time.

Applicants contend that the portion of the method characterized as a "mental step" should be given weight in establishing novelty. The Examiner appears to agree that the '497 patent does not include such a mental step. In fact the '497 patent is silent with respect to whether any ephs or ephrins are primarily expressed on arterial or venous cells. Furthermore, the '497 patent is silent with respect to any role in angiogenesis of any ephrin other than ephrin B1 and ephrin A1 and any eph other than eph B1 and eph A2. There is no mention of any eph or ephrin that is primarily expressed in either arterial or venous cells. Accordingly, the '497 patent does not anticipate the claims explicitly or implicitly. Nonetheless, in order to expedite prosecution, claims 46 and 49 are amended to recite "at least a portion of an ephrin ligand that is selectively expressed on one of either venous or arterial cells" and "at least a portion of an eph ligand that is selectively expressed on one of either arterial or venous cells". It is Applicants' belief that this amendment is merely a clarification of the "mental step" in the claims as previously presented and does not constitute a narrowing amendment for reasons related to patentability.

Claims 77-82, 84, 85, 114, 120 and 153 depend from claims 46 and/or 49 are also not anticipated for the same reasons. In addition, these dependent claims contain further elements that are not disclosed by the '497 patent, however, given the novelty of the independent claims, no further argument on this point is deemed necessary at this time.

Applicants respectfully request reconsideration of all rejections under 35 U.S.C. § 102(e) in view of the '497 patent.

#### **U.S. Patent No. 6,413,730 to Holland et al. (the '730 patent)**

The Examiner has rejected claims 47, 50, 80, 81, 88, 89, 92, 95-100, 107, 108 and 152 as anticipated by the '730 patent under 35 U.S.C. § 102(e). The '730 patent was filed in the U.S. under § 371 and accorded a section 371 date of Mar. 12, 1999; the PCT application was accorded an international filing date of Jul. 4, 1997 and published Jan. 15, 1998; a U.S. provisional application was filed Jul. 5, 1996.

The Examiner argues that, “the ‘730 patent teaches ephrin B2 as a ligand for eph B4. Methods for identifying inhibitors and activators of the interaction of receptor and ligand, as claimed in instant claims 47 and 50, are taught in column 2, lines 11-34 and claimed in claims 1 and 5.”

Applicants respectfully disagree with this rejection on the grounds that the ‘730 patent does not disclose all the elements of the claims, particularly the claims as amended. In addition, because the international filing date was prior to November on Oct. 1, 1998, the patent only has a 102(e) date as of the 371 date, which is March 12, 1999. Therefore, this patent cannot be used as a proper basis for a rejection under 102(e). The PCT application might, if identical to the issued U.S. patent, be used in a rejection under 102(a) with a date of Jan. 15, 1998. Applicants reserve the right to analyze the PCT publication and, if needed, file a Declaration under 37 CFR 1.131 to demonstrate invention prior to Jan. 15, 1998. Applicants believe such measures to be unnecessary given that the ‘730 patent, and presumably the parent PCT, does not anticipate the pending claims.

The ‘730 patent is silent with respect to any involvement of ephrin B2 and eph B4 in angiogenesis or in any biological process that is regulated by the ephrin B2- eph B4 interaction. The ‘730 patent is also silent with respect to any selective expression of ephs or ephrins. Nonetheless, in order to expedite prosecution, claims 47 and 50 are amended so as to relate to angiogenesis. Accordingly, the amended claims are not anticipated by the ‘730 patent.

Claims 80, 81, 88, 89, 92, 95-100, 107, 108 and 152 depend from claim 47 and/or claim 50 and are also not anticipated by the ‘730 patent for the same reasons. In addition, these dependent claims contain further elements that are not disclosed by the ‘730 patent, however no further argument on this point is deemed necessary at this time.

Applicants respectfully request reconsideration of all rejections under 35 U.S.C. § 102(e) in view of the ‘730 patent.

### **III. THE CLAIMED SUBJECT MATTER IS NOT OBVIOUS IN VIEW OF THE ART**

Claims 83, 86, 154 and 155 are rejected under 35 U.S.C. § 103(a) as unpatentable over the '497 patent in view of, variously, Pandey et al., Science, 1996, vol. 268, pp. 567-569, the '730 patent or the general knowledge of one of ordinary skill in the art.

As described above, the '497 patent fails to disclose that any eph or ephrin would be primarily expressed on an arterial or venous cell. This defect is not corrected by Pandey et al., the '730 patent or the general knowledge in the art at the time of filing. Accordingly, these claims cannot be rendered obvious by any of these combinations of references and knowledge.

Applicants respectfully request reconsideration and withdrawal of all rejections under 35 U.S.C. § 103(a).

### **IV. AMENDMENT TO CLAIMS 156 AND 157**

Claims 156 and 157 are amended to include the term "comprising" as requested by the examiner. Applicants request allowance of these claims.


### **CONCLUSION**

In view of the foregoing amendments and remarks, Applicants submit that the pending claims are in condition for allowance. Early and favorable reconsideration is respectfully solicited. The Examiner may address any questions raised by this submission to the undersigned at 617-951-7000. Applicants hereby request that any fee required for timely consideration of this submission be charged to **Deposit Account No. 18-1945**.

Respectfully Submitted,

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